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(purged)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

T1393M

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER

NOV 19 1997

VIA FEDERAL EXPRESS

Mr. Shigeki Tanaka
Senior Managing Director
Nissho Corporation
3-9-3 Honjo-Nishi, Kita-Ku
Osaka, 531, Japan

Dear Mr. Tanaka:

During the Food and Drug Administration's (FDA) inspection of your firm, Nissho Corporation, Ohdate Factory, located at 8-7 Hanukiyachi, Nida, Ohdate City, Akita, Japan from September 1-5, 1997, our investigator determined that your firm manufactures hollow fiber dialyzers. Hollow fiber dialyzers are devices within the meaning of Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated, in that the methods used in, or the facilities or controls used for the manufacture, packaging, storage, or installation are not in conformance with the Quality System Regulations, as specified in Title 21, Code of Federal Regulations (21 CFR), Part 820, as follows:

1. Failure to identify action(s) needed to correct and prevent recurrence of nonconforming products as required by 21 CFR 820.100(a)(3). For example:

   a. [redacted] complaints were received for devices CA and CT dialyzers distributed in the United States ([redacted]) between April 1995 and March 1997. Failure investigation indicated several causes for the [redacted] problem. One such cause identified was the use of [redacted] during the [redacted] process for [redacted] which reduced the [redacted] of the product. Since June 1996, your firm has no longer used the [redacted] during the [redacted] process, but even with the use of only [redacted] of the [redacted] and [redacted] of the [redacted] were found to have [redacted] during the internal testing.

   b. Example of inadequate/incomplete failure investigation for this problem was also identified during the inspection. Although during the failure investigation, the firm proposed an immediate corrective action such as [redacted] (another factor identified as a cause of the [redacted]), there was no documentation to support that the process had been implemented. Other corrective actions involving [redacted] such as change in the [redacted] and change in the [redacted] were proposed, but there was no evidence of validation or implementation of these actions by close of the inspection.

There appears to be no evidence that an adequate corrective action has been identified by the firm regarding the [redacted] problem .

Your response to FDA 483 items 1 and 2 includes identification of the causes [redacted] reported in the United States, summary of the investigation on this problem, and future corrective actions/documentation to be implemented by the firm. Your response also stated the test results noted were produced on purpose. Documentation of protocols and procedures used to accomplish testing methods were not supplied. This response is considered inadequate.

c. For the [redacted] complaints of [redacted] complaints in dialyzers shipped to the United States, there was no documentation of investigation of manufacturing processes, method of inspections, possible corrective actions, or evaluation of effectiveness of corrective action to determine the cause of this problem. Representatives of your firm had reportedly stated that they were conducting a close inspection of the manufacturing processes. Although causes such as [redacted] and [redacted] in [redacted] were thought to be causes of the [redacted] the nature of these causes specifically relating to manufacturing process was not identified or documented.

Your response to the FDA 483 is inadequate in that copies of referenced revised procedures/protocols were not provided with the response.

d. [redacted] data was not analyzed to identify specific failure causes. For example, of [redacted], it is not known how many [redacted] were due to [redacted] or [redacted] This incomplete data would make it difficult for your firm to determine existing or potential causes of nonconforming products or other quality problems.

Your firm's response to this item was the proposal of the implementation of a new procedure (draft provided with the response) which would reportedly collect sufficient data that would be useful for trending, corrective and preventive action, etc. This response appears adequate.

2. Failure to validate or verify the corrective action to ensure that such action is effective and not adversely affect the finished device as required by 21 CFR 820.100 (a)(4).

a. For example, your firm identified that the [redacted] in the [redacted] process may be the cause of a [redacted] resulting in [redacted], and changed the process without formal documentation or validation of the change. Your firm did not confirm whether the problem identified and "corrected " was the cause of the [redacted] or if the change affected the finished device in any way.

Your firm's response to this item was not addressed.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

We acknowledge that you have submitted a response, dated October 3, 1997, concerning our investigator's observations noted on the form FDA 483. We have reviewed your response and are unable to fully evaluate the adequacy of your response. In order to evaluate your response to the FDA 483, it will be necessary for you to submit copies of your modified protocols/procedures and results referenced in your response.

You should take prompt action to correct these and any other manufacturing or quality systems deviations identified by your internal audits. Failure to promptly correct these deviations may be identified in a follow-up inspection, and may result in the detention of your device(s) without physical examination upon entry into the United States.

Please notify this office, in writing, within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If the documentation is not in English, please provide a translation to facilitate our review. Please address your response and any questions to Mr. Timothy R. Wells, Chief, OB/GYN, Gastroenterology and Urology Branch, at the letterhead address.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Ms. Sharon Murrain-Ellerbe at the letterhead address or at (301) 594-4616 or FAX (301)594-4638.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health